Flovent HFA Product Profile Summary

This information is provided in response to your request for information about Flovent® HFA (fluticasone propionate).

DISEASE: CONSENSUS TREATMENT GUIDELINES FOR ASTHMA

- National asthma management guidelines recommend the use of low-dose inhaled corticosteroids (ICS) as the preferred therapy for all patients with mild persistent asthma. Additionally, the use of an ICS either alone or in combination with adjunctive therapy is recommended as a preferred therapy for all severities of persistent asthma.(1)

BENEFITS OF *FLOVENT HFA* IN ASTHMA

- *Flovent HFA* Inhalation Aerosol contains the potent corticosteroid fluticasone propionate that helps to reduce inflammation in the airways, one of the main components of asthma.(2)
- *Flovent HFA* is available as pressurized, metered dose aerosol units for oral inhalation that delivers per actuation either 44, 110 or 220 mcg ex-actuator of a microcrystalline suspension of fluticasone propionate in an hydrofluoroalkane (HFA) propellant. It contains no excipients, soya lecithin, or chlorofluorocarbon (CFC) propellants.
- *Flovent HFA* is fitted with a dose counter that keeps track of the number of inhalations remaining, helping the patient to know when it is time for a prescription refill.
- The fluticasone propionate in *Flovent HFA* has negligible oral bioavailability (<1%) due to incomplete absorption from the gastrointestinal tract and extensive first-pass metabolism by the liver.
- *Flovent HFA* has 30% and 55% lower systemic exposure in healthy adults and children with asthma, respectively, compared with *Flovent* CFC.
- *Flovent HFA* provided an onset of effect on Day 1 for all 3 strengths with significant improvement in FEV_1 noted at Week 1, the first spirometry analysis time-point, compared with placebo. Maximum benefit may not be achieved for 1 to 2 weeks or longer.
- *Flovent HFA* is approved for use in children 4 years of age and older with asthma.
- *Flovent HFA* is also indicated for patients requiring oral corticosteroid therapy for asthma. Many of these patients may be able to reduce or eliminate their requirement for oral corticosteroids over time.

EFFICACY OF *FLOVENT HFA* IN ASTHMA

- Three 12 to 16-week US pivotal trials in 980 adolescent (≥12 years old) and adult patients with asthma evaluated the efficacy and safety of *Flovent HFA*.(2,3,4) Patients receiving *Flovent HFA* had greater improvements in lung function, asthma symptom scores, and use of rescue albuterol compared to the placebo group. In Study 3, *Flovent HFA* enabled more patients (59% and 56% in the groups treated with *Flovent HFA* 440 and 880 mcg, respectively, twice daily) to eliminate oral prednisone as compared to placebo (13%).
- Two long-term studies of 6 months and 1 year duration showed that efficacy was maintained throughout the duration of the studies in patients receiving *Flovent HFA* . None of the patients were withdrawn due to lack of efficacy. The pattern of adverse events was similar to that observed in the 12-week studies.(2)
- A 12-week clinical trial evaluated the safety and efficacy of *Flovent HFA* 88 mcg twice daily in 241 children 4 to 11 years of age.(5) *Flovent HFA* improved peak expiratory flow, reduced daily rescue albuterol use, and reduced nighttime awakenings compared to placebo. Additionally, the safety and efficacy of *Flovent HFA* in children is supported by adequate and well-controlled studies in patients 12 years of age and older, pharmacokinetic studies in children 4 to 11 years old, and the established efficacy of other inhaled formulations of *Flovent* in children 4 to 11 years of age.(2)
- In 4 head-to-head comparative clinical trials in adolescent and adult patients, *Flovent HFA* was clinically equivalent to *Flovent* CFC at the same doses. (6,7) (8) (9)

SAFETY OF *FLOVENT HFA*

- Particular care is needed for patients who are transferred from systemic corticosteroids to *Flovent HFA* because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids. Particular care should be taken in observing patients post-operatively or during periods of stress for evidence of inadequate adrenal response.(2)
- Co-administration of fluticasone propionate and ritonavir (a highly potent cytochrome P450 3A4 inhibitor) is not recommended unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects.
- *Flovent HFA* is not a bronchodilator and is not indicated for rapid relief of bronchospasm.
- Patients treated with *Flovent HFA* should be observed carefully for any evidence of systemic corticosteroid effects. It is possible that systemic corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients, particularly when *Flovent HFA* is administered at higher than recommended doses over a prolonged period of time.
- Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. A 52-week, placebo-controlled US study assessed the potential growth effects of *Flovent* inhalation powder 50 and 100 mcg BID, via *Diskhaler* in 325 prepubescent children 4 to 11 years of age. A subset analysis of children who remained pre-pubertal during the study revealed growth rates of 6.10 (placebo; n = 57), 5.91 (50 mcg; n = 74), and 5.67 cm/year (100 mcg; n = 79). The clinical significance of these growth data is not certain. The growth of children and adolescents receiving orally inhaled corticosteroids, including *Flovent HFA*, should be monitored routinely (e.g., via stadiometry).
- Rare instances of glaucoma, increased intraocular pressure, and cataracts have been reported in patients following the long-term administration of inhaled corticosteroids, including *Flovent*.

- In clinical studies with *Flovent*, the development of localized infections of the pharynx with Candida albicans has occurred.
- Adverse events in clinical trials with *Flovent HFA* were similar to placebo.
- Adverse events with *Flovent HFA* were similar to placebo. The most common adverse events (>5%) reported in clinical trials with *Flovent HFA* 44, 110, and 220 mcg twice daily, respectively (and placebo) in patients ≥12 years of age were: upper respiratory tract infection – 18%, 16%, 16% (14%), throat irritation – 8%, 8%, 10% (5%), sinusitis/sinus infection – 6%, 7%, 4%, (3%), hoarseness/dysphonia – 2%, 3%, 6%, (<1%), cough – 4%, 6%, 4%, (5%), bronchitis – 2%, 2%, 6%, (5%), and headache – 11%, 7%, 5%, (6%).

INDICATIONS FOR *FLOVENT HFA*

- *Flovent HFA* is indicated for the maintenance treatment of asthma as prophylactic therapy in patients 4 years of age and older. It is also indicated for patients requiring oral corticosteroid therapy for asthma. Many of these patients may be able to reduce or eliminate their requirement for oral corticosteroids over time. *Flovent HFA* is not indicated for the relief of acute bronchospasm.[(2)]

DOSING FOR *FLOVENT HFA*

- The recommended dosages of *Flovent HFA* for patients ≥ 12 years were based on prior asthma therapy Table 1. The recommended pediatric dosage is 88 mcg twice daily regardless of prior therapy. After asthma stability has been achieved, it is always desirable to titrate to the lowest effective dosage to reduce the possibility of side effects.

Table 1. Recommended Dosages for *Flovent HFA*[(2)]

	Recommended Starting Dosage	**Highest Recommended Dosage**
Pediatric 4 to 11 years*	88 mcg twice daily	88 mcg twice daily
Patients ≥12 years		
Bronchodilators alone	88 mcg twice daily	440 mcg twice daily
Inhaled corticosteroids	88 - 220 mcg twice daily	440 mcg twice daily
Oral corticosteroids	440 mcg twice daily	880 mcg twice daily

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